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Pharyngolaryngeal ulcers associated with the improper use of alendronate

Hiroshi Sakaida [a,*], Hiroto Yuasa [b], Kazuo Fukutome [b], Kazuhiko Takeuchi [a]

[a] Department of Otorhinolaryngology – Head & Neck Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan
[b] Department of Oncologic Pathology, Mie University Graduate School of Medicine, Tsu, Mie, Japan

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ABSTRACT

Bisphosphonates can cause mucosal irritation. Although esophageal ulceration is a well-recognized adverse effect of bisphosphonates, pharyngolaryngeal ulcers associated with the improper use of oral bisphosphonates have rarely been described. A previously healthy 78-year-old woman presented with refractory pharyngolaryngeal ulcers. Extensive evaluation, including biopsy, bacterial culture, and blood tests did not identify any findings that indicated a specific disease diagnosis. Antibiotics and oral prednisolone were ineffective. Ultimately, it was found that the patient regularly took a tablet of alendronate, a type of bisphosphonate, by dissolving it in the oral cavity. Within 2 weeks after withdrawal of the use of the medication, her symptoms were eliminated, and the lesions were completely healed. This case illustrates the importance of correct administration of bisphosphonates. Given the widespread use of bisphosphonates, physicians need to be aware that their improper use can cause pharyngolaryngeal ulcers.

1. Introduction

Bisphosphonates, a class of selective inhibitors of osteoclast-mediated bone resorption, are widely used for the treatment and prevention of osteoporosis [1] and for the treatment of Paget's disease of the bone [2]. Bisphosphonates are well-tolerated, but they are known to cause several adverse effects, of which most notable are osteonecrosis of the jaw [3] and mucositis and ulceration of the esophagus [4]. The latter conditions result from prolonged local mucosal exposure to the medication [4]. Therefore, patients are instructed to take the medication in a correct manner to prevent these adverse consequences. Chewing the medication should also be avoided to prevent similar adverse reactions from occurring in the mouth and pharynx. To date, only 12 cases of oral ulcers due to improper use of bisphosphonates have been reported [5]. Here, we report a 78-year-old woman with pharyngolaryngeal ulcers due to improper use of alendronate, a type of bisphosphonate. This case highlights the importance of correct administration of bisphosphonates and the need for knowledge concerning their adverse effects.

2. Case report

A 78-year-old woman was referred to our clinic because of ulcerative lesions located in the hypopharynx, mesopharynx, and larynx, which persisted for one month despite administration of oral antibiotics. The patient had begun to feel a sore throat 2 months prior to the presentation but reported no bleeding, cough, or other symptoms. The patient had no history of dysphagia. Her medical history was notable for osteoporosis due to aging, and the patient had been taking once a week a tablet of 35 mg of alendronate sodium manufactured by a generic pharmaceutical company. On examination, the patient was afebrile and clinically stable. Endoscopic examination was

* *Corresponding author at*: Department of Otorhinolaryngology – Head & Neck Surgery, Mie University Graduate School of Medicine, Tsu, Mie 514-8507, Japan. Fax: +81 59 232 9582.
E-mail address: hsakaida@clin.medic.mie-u.ac.jp (H. Sakaida).

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performed using the Olympus Visera Elite video endoscopy system with a high-definition otolaryngological endoscope (ENF-VH video endoscope with a CLV-S190 xenon light source, and OTV-S190 video processor; Olympus Medical Systems, Tokyo, Japan). White light endoscopy revealed irregularly shaped lesions covering the right pyriform sinus, a part of the epiglottis, and the vallecula (Fig. 1A). Endoscopy with narrow band imaging (Olympus Medical Systems, Tokyo, Japan) demonstrated no microvascular irregularities known as intra-epithelial papillary capillary loops in the lesions (Fig. 1B). There were no abnormalities in either the oral cavity, nasal cavity, or epipharynx. No sign of osteonecrosis of the jaw was evident. The patient did not have any ocular or cutaneous manifestations suggestive of Behçet's disease. Blood tests were normal, and autoantibodies, such as against desmoglein 3 and desmoglein 1, were negative. Bacterial culture from the lesions yielded normal flora. The patient underwent a biopsy from the lesions, which demonstrated severe inflammatory reactions with a dense infiltration of neutrophils into the submucosal tissue

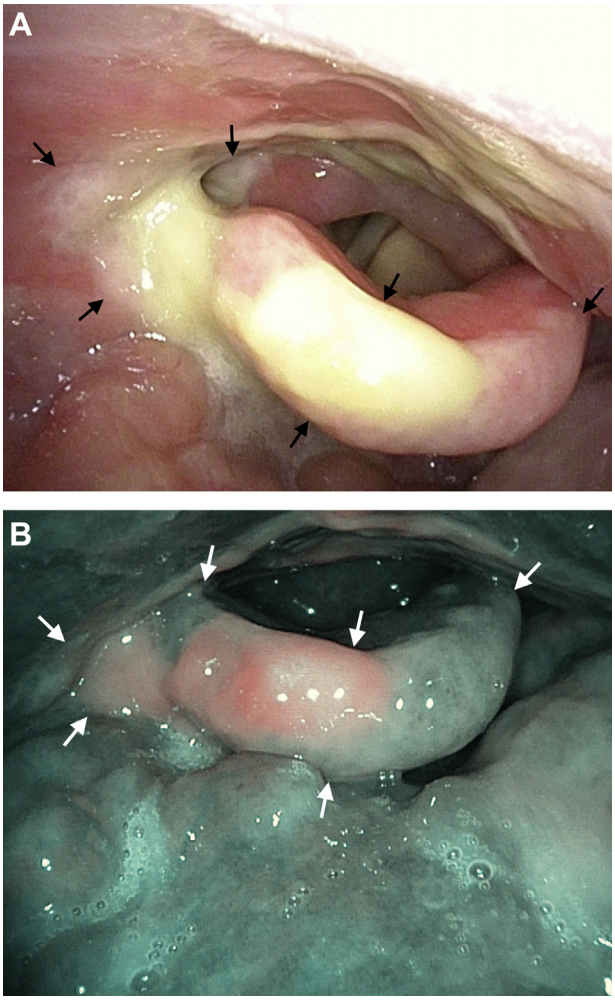

Fig. 1. (A) White light endoscopic view showing irregularly shaped lesions covering the right pyriform sinus, a part of the epiglottis, and the vallecula. The lesions were covered with a layer of white plaques (black arrows) and varied in shape at each visit. There was no bleeding or mass associated with the lesions. (B) Laryngoscopy with narrow band imaging showing the ulcerative lesions (white arrows). There were no microvascular irregularities known as intra-epithelial papillary capillary loops.

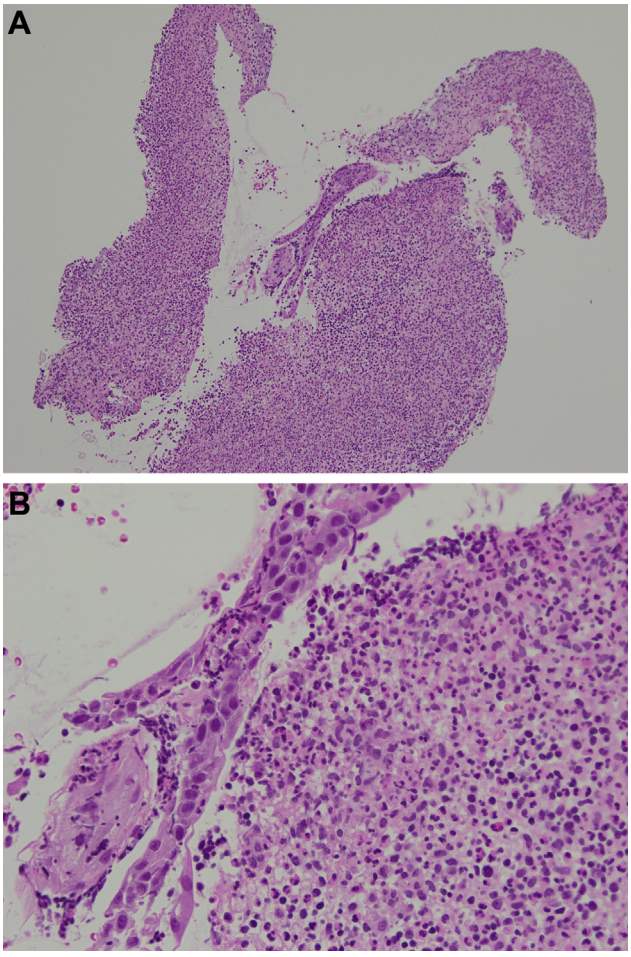

Fig. 2. Histopathological findings of a biopsy specimen obtained from the lesions (hematoxylin and eosin stain, original magnification 100× (A), 400× (B)). Severe inflammatory reactions with dense infiltration of neutrophils into the submucosal tissue were seen. There were no specific pathological findings or malignancies.

(Fig. 2A and B). Most of the epithelial layer of the specimen was missing. There was no evidence of either specific pathological findings or malignancies. A tentative diagnosis of refractory pharyngolaryngeal ulcer was made, and a one-week course of oral prednisolone (10 mg/day) was administrated without success. We performed a second biopsy, which yielded the same result as previously found. Contrast-enhanced computed tomography showed no obvious abnormalities in the head and neck region.

At her sixth visit to our outpatient clinic, the patient still remained symptomatic, with no improvement on endoscopic findings that were variable in shape at each visit (Fig. 3). A daughter of the patient reported that the patient regularly took a tablet of alendronate by dissolving it without water in the oral cavity and then swallowing it. Improper use of alendronate was thought to be the cause of her lesions, and we advised the patient to discontinue taking the medication. The patient underwent esophagogastroduodenoscopy, which revealed no findings consistent with the adverse effects of alendronate. Within 2 weeks after discontinuing the alendronate, her symptoms were no longer present, and her pharyngolaryngeal ulcers had healed with resultant mild scar formation (Fig. 4).

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